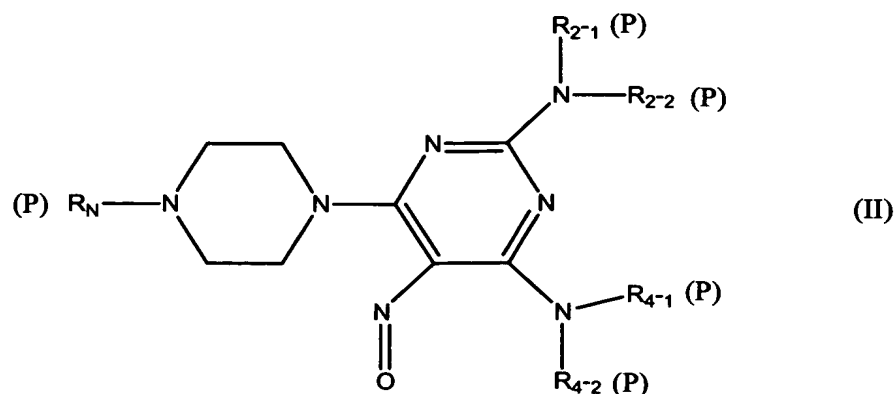


CLAIM

1. A piperazinyl pyrimidinyl nitroso compound of the formula (II)



5

where (P)-R<sub>N</sub> is:

-N=O,

(P)-R<sub>N-1</sub>-O-OC-(CH<sub>2</sub>)<sub>n1</sub>- where n<sub>1</sub> is 1 thru 6 and where (P)-R<sub>N-1</sub> is H- or C<sub>1</sub>-C<sub>4</sub>

alkyl,

10

C<sub>1</sub>-C<sub>6</sub> alkyl,

where (P)-R<sub>2-1</sub> is:

-N=O and

C<sub>1</sub>-C<sub>6</sub> alkyl;

where (P)-R<sub>2-2</sub> is:

15

C<sub>1</sub>-C<sub>6</sub> alkyl; and

where (P)-R<sub>2-1</sub> and (P)-R<sub>2-2</sub> are taken together with the attached nitrogen atom to form a ring selected from the group consisting of:

pyrrolidinyl,

piperidinyl,

20

homopiperidinyl,

morpholinyl,

4-nitroso-1-piperazinyl;

where (P)-R<sub>4-1</sub> is

-N=O and

C<sub>1</sub>-C<sub>6</sub> alkyl; and

where (P)-R<sub>4-2</sub> is

C<sub>1</sub>-C<sub>6</sub> alkyl; and

where (P)-R<sub>4-1</sub> and (P)-R<sub>4-2</sub> are taken together with the attached nitrogen atom to form

5 a ring selected from the group consisting of:

pyrrolidinyl,

piperidinyl,

homopiperidinyl,

morpholinyl,

10 4-nitroso-1-piperazinyl; and pharmaceutically acceptable salts thereof.

2. A piperazinyl pyrimidinyl nitroso compound according to claim 1 where the variable substituents (P)-R<sub>2-1</sub> and (P)-R<sub>2-2</sub> are the same as the variable substituents (P)-R<sub>4-1</sub> and (P)-R<sub>4-2</sub>.

15

3. A piperazinyl pyrimidinyl nitroso compound according to claim 1 where (P)-R<sub>2-1</sub> and (P)-R<sub>2-2</sub>, and (P)-R<sub>4-1</sub> and (P)-R<sub>4-2</sub> are both taken together with the attached nitrogen atom to form pyrrolidinyl.

20 4. A piperazinyl pyrimidinyl nitroso compound according to claim 1 which contains 3 -N=O groups.

5. A piperazinyl pyrimidinyl nitroso compound according to claim 1 which contains 4 -N=O groups.

25

6. A piperazinyl pyrimidinyl nitroso compound according to claim 1 where the pharmaceutically acceptable salt is selected from the group consisting of salts of the following acids acetic, aspartic, benzenesulfonic, benzoic, bicarbonic, bisulfuric, bitartaric, butyric, calcium edetate, camsyllic, carbonic, chlorobenzoic, citric, edetic, edisylic, estolic, esyl, esylic, formic, fumaric, gluceptic, gluconic, glutamic, glycollylarsanilic, hexamic, hexylresorcinoic, hydrabamic, hydrobromic, hydrochloric, hydroiodic, hydroxynaphthoic, isethionic, lactic, lactobionic, maleic, malic, malonic, mandelic, methanesulfonic,

methylnitric, methylsulfuric, mucic, muconic, napsylic, nitric, oxalic, p-nitromethanesulfonic, pamoic, pantothenic, phosphoric, monohydrogen phosphoric, dihydrogen phosphoric, phthalic, polygalactouronic, propionic, salicylic, stearic, succinic, succinic, sulfamic, sulfanilic, sulfonic, sulfuric, tannic, tartaric, teoclic and toluenesulfonic.

5

7. A piperazinyl pyrimidinyl nitroso compound according to claim 1 where (P)-R<sub>N</sub> is -N=O.

8. A piperazinyl pyrimidinyl nitroso compound according to claim 7 where the substituted  
10 pyrimidinyl nitroso compound is

5-nitroso-2,4-di(1-pyrrolidinyl)-6-(4-nitroso-1-piperazinyl)pyrimidine.

9. A piperazinyl pyrimidinyl nitroso compound according to claim 1 where (P)-R<sub>N</sub> is (P)-R<sub>N-1</sub>-O-OC-(CH<sub>2</sub>)<sub>n1</sub>-.

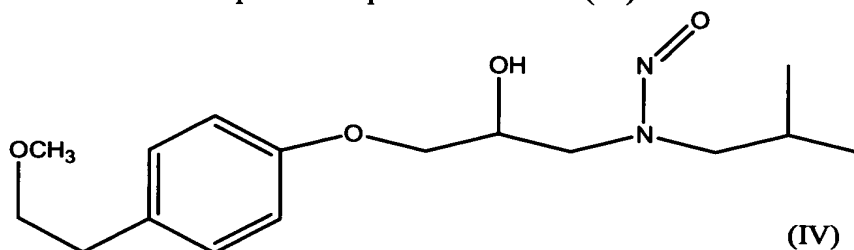
15

10. A piperazinyl pyrimidinyl nitroso compound according to claim 9 where the piperazinyl pyrimidinyl nitroso compound is

5-nitroso-2,4-di(1-pyrrolidinyl)-6-[4-(3-propionic acid methyl ester)piperazin-1-yl]pyrimidine.

20

11. N-nitrosometoprolol compound of formula (IV)



and pharmaceutically acceptable salts thereof.

25

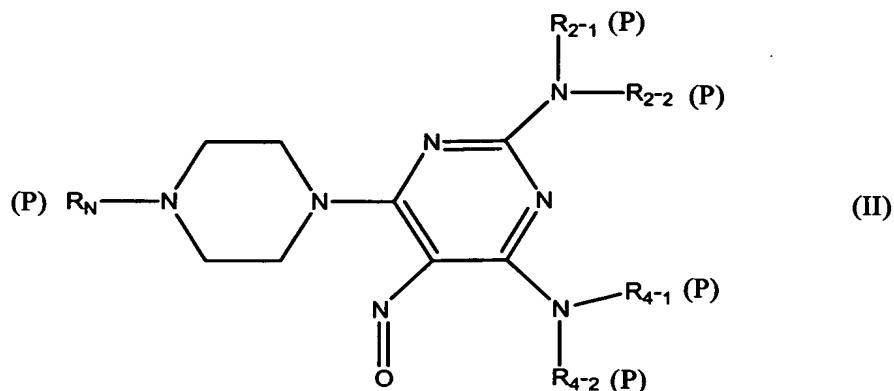
12. N-nitrosometoprolol compound (IV) according to claim 11 where the pharmaceutically acceptable salt is selected from the group consisting of salts of the following acids acetic, aspartic, benzenesulfonic, benzoic, bicarbonic, bisulfuric, bitartaric, butyric, calcium edetate,

TOL01 P-100A

camrylic, carbonic, chlorobenzoic, citric, edetic, edisyllic, estolic, esyl, esylic, formic, fumaric, gluceptic, gluconic, glutamic, glycolylarsanilic, hexamic, hexylresorcinoic, hydrabamic, hydrobromic, hydrochloric, hydroiodic, hydroxynaphthoic, isethionic, lactic, lactobionic, maleic, malic, malonic, mandelic, methanesulfonic, methylnitric, methylsulfuric, mucic, muconic, napsylic, nitric, oxalic, p-nitromethanesulfonic, pamoic, pantothenic, phosphoric, monohydrogen phosphoric, dihydrogen phosphoric, phthalic, polygalactouronic, propionic, salicylic, stearic, succinic, succinic, sulfamic, sulfanilic, sulfonic, sulfuric, tannic, tartaric, teoclic and toluenesulfonic.

- 10 13. A method of treating a human who has an ischemic disease selected from the group consisting of coronary heart disease, stroke, hemorrhagic shock, peripheral vascular disease (upper and lower extremities) and transplant related injuries and who is in need of treatment which comprises administering to that human an anti-ischemic effective amount of a

15



where (P)-R<sub>N</sub> is:

20

-N=O,

(P)-R<sub>N-1</sub>-O-OC-(CH<sub>2</sub>)<sub>n1</sub>- where n<sub>1</sub> is 1 thru 6 and where (P)-R<sub>N-1</sub> is H- or C<sub>1</sub>-C<sub>4</sub> alkyl,

C<sub>1</sub>-C<sub>6</sub> alkyl,

where (P)-R<sub>2-1</sub> is:

TOL01 P-100A

-N=O and

C<sub>1</sub>-C<sub>6</sub> alkyl;

where (P)-R<sub>2.2</sub> is:

C<sub>1</sub>-C<sub>6</sub> alkyl; and

5 where (P)-R<sub>2.1</sub> and (P)-R<sub>2.2</sub> are taken together with the attached nitrogen atom to form a ring selected from the group consisting of:

pyrrolidinyl,

piperidinyl,

homopiperidinyl,

10 morpholinyl,

4-nitroso-1-piperazinyl;

where (P)-R<sub>4.1</sub> is

-N=O and

C<sub>1</sub>-C<sub>6</sub> alkyl; and

15 where (P)-R<sub>4.2</sub> is

C<sub>1</sub>-C<sub>6</sub> alkyl; and

where (P)-R<sub>4.1</sub> and (P)-R<sub>4.2</sub> are taken together with the attached nitrogen atom to form a ring selected from the group consisting of:

pyrrolidinyl,

20 piperidinyl,

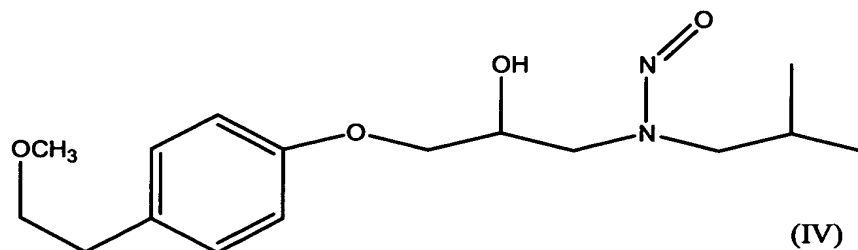
homopiperidinyl,

morpholinyl,

4-nitroso-1-piperazinyl;

or N-nitrosometoprolol of formula (IV)

25



and pharmaceutically acceptable salts thereof.

14. A method of treating a human who has an ischemic disease according to claim 13 where the administering is IV or oral.

5 15. A method of treating a human who has an ischemic disease according to claim 13 where the IV anti-ischemic effective amount is from about 5 to about 100 mg/kg/dose.

16. A method of treating a human who has an ischemic disease according to claim 13 where the oral anti-ischemic effective amount is from about 5 to about 50 mg/kg/dose.

10

17. A method of treating a human who has an ischemic disease according to claim 13 where the compound is a piperazinyl pyrimidinyl nitroso compound of formula (II).

18. A method of treating a human who has an ischemic disease according to claim 17 where  
15 the piperazinyl pyrimidinyl nitroso compound (II) is

5-nitroso-2,4-di(1-pyrrolidinyl)-6-(4-nitroso-1-piperazinyl)pyrimidine or

5-nitroso-2,4-di(1-pyrrolidinyl)-6-[4-(3-propionic acid methyl ester)piperazin-1-yl]pyrimidine

20